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CHAGASIC MENINGOENCEPHALITIS: CASE REPORT OF A RECENTLY INCLUDED AIDS-DEFINING ILLNESS IN BRAZIL

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SUMMARY

Recently, reactivation of Chagas disease (meningoencephalitis and/or myocarditis) was included in the list of AIDS-defining illnesses in Brazil. We report a case of a 52-year-old patient with no history of previous disease who presented acute meningoencephalitis. Direct examination of blood and cerebrospinal fluid (CSF) showed *Trypanosoma cruzi*. CSF culture confirmed the diagnosis. Serological assays for *T. cruzi* and human immunodeficiency virus (HIV) were positive. Despite treatment with benznidazol and supportive measures, the patient died 24 hours after hospital admission. In endemic areas, reactivation of Chagas disease should always be considered in the differential diagnosis of meningoencephalitis among HIV-infected patients, and its presence is indicative of AIDS.

KEYWORDS: Chagas disease; Meningoencephalitis; Central nervous system; Epidemiology; Acquired immunodeficiency syndrome; Brazil.

INTRODUCTION

Chagas disease or American trypanosomiasis is endemic in Latin America and is caused by the flagellated protozoan *Trypanosoma cruzi*, and generally transmitted to humans by triatomine dejections. It can also be transmitted through blood transfusions and contaminated hemoderivates, needles and by syringe sharing among intravenous drug users, besides congenital transmission[9,25].

Globally, Chagas disease represents the third most important tropical disease, after malaria and schistosomiasis[20]. In the Americas, there have been successful experiences regarding the control of Chagas disease vectorial transmission. Nevertheless, there are an estimated 11 million chronic cases of infection by *T. cruzi*[13]. In Brazil, some 3 to 5 million individuals are infected and, despite important progress achieved in recent years, there are still isolated reports of acute cases[4,10], and also of blood transmission through intravenous drug users in several states and regions (Rio Grande do Sul, Minas Gerais, and Northeast)[13,16,19,20,25]. The progressive increase of Chagas disease cases in urban populations, as a result of massive migration from rural areas to major cities, associated to the interiorization of the epidemic infection caused by the human immunodeficiency virus (HIV)[7], have created the conditions for emergence of a higher number of co-infection cases. Consequently, in the presence of severe immunodeficiency there is a possibility of chronic Chagasic infection reactivation, which is manifested by severe forms of neurological (75 - 90% of cases) or myocardial (30% of cases) involvement[15,18-20,24,25,27].

Several studies have demonstrated the opportunistic nature of Chagas disease reactivation in AIDS patients[9,12,14-18,28], which suggests that it should be considered an AIDS-defining illness[1,11,20,26]. Despite that established by the Centers for Disease Control and Prevention[8], the Brazilian Ministry of Health has recently included reactivation of Chagas disease (meningoencephalitis and/or myocarditis) in the list of AIDS-defining events[6]. The potential advantages of this decision, include improved surveillance of HIV-associated Chagas disease, increased number of studies related to this co-infection, and provision of social benefits for the affected patients[1].

In this study, we report a case of chagasic meningoencephalitis that led to the diagnosis of HIV infection, and which defined AIDS.

CASE REPORT

A 52-year-old heterosexual male was admitted to the hospital with a seven-day history of fever, headache and asthenia, and three days with altered level of consciousness. He had lost approximately 30 kg weight during the previous year. His medical history was unremarkable, as well as the use of intravenous drugs and blood transfusions. He had spent his childhood and adolescence in a rural area in Bahia but has lived continuously in an urban area of São Paulo for 33 years prior to becoming ill. On physical examination, he presented fever (38.5 ºC), hypotension (90/60 mmHg), tachycardia, tachydyspneia, neck stiffness, and mental state alterations. Pulmonary auscultation revealed bilateral crepitation. He did not present papilledema, lateralizing signs (e.g. hemiparesis or

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hemianoptic field defect), or focalizing signs (e.g. aphasia). A blood count revealed hemoglobin = 13.3 mg/dL and leukocytes = 10,200 cells/mm^3 (92% neutrophils, 7% lymphocytes, 1% monocytes). Biochemical test did not detect any alterations. Due to the severity of illness it was not possible to perform brain computed tomography (CT). A careful lumbar puncture was performed which found 16 cells (94% lymphocytes, 4% monocytes, 1% neutrophils, 1% eosinophils), protein 721 mg/dL, and glucose 0 mg/dL. Direct examination of CSF showed numerous forms of *T. cruzi* trypomastigote (Fig. 1), and CSF culture confirmed the diagnosis. Blood and CSF cultures for bacteria, fungi, and mycobacteria showed no growth. Serological assays for *T. cruzi* (indirect immunofluorescence, passive hemagglutination and enzyme linked immunoassay (ELISA)) were reagent. The xenodiagnosis was positive. A rapid test for HIV was reagent, which was later confirmed with ELISA and Western Blot. Benznidazol 5mg/kg/day twice daily was initiated. The patient was transferred to the Intensive Care Unit and placed under mechanical ventilation and hemodynamic support. Despite these measures, the patient developed neurological deterioration and multiple organ failure (respiratory insufficiency, oligoanuria, and shock) and died 24 hours after admission. Necropsy revealed findings compatible with brain edema, meningoencephalitis and an extensive area of necrosis in the right cerebellar region. Signs of dilated myocardiopathy and bilateral pulmonary congestion were observed. There were no findings of megacolon or megaesophagus.

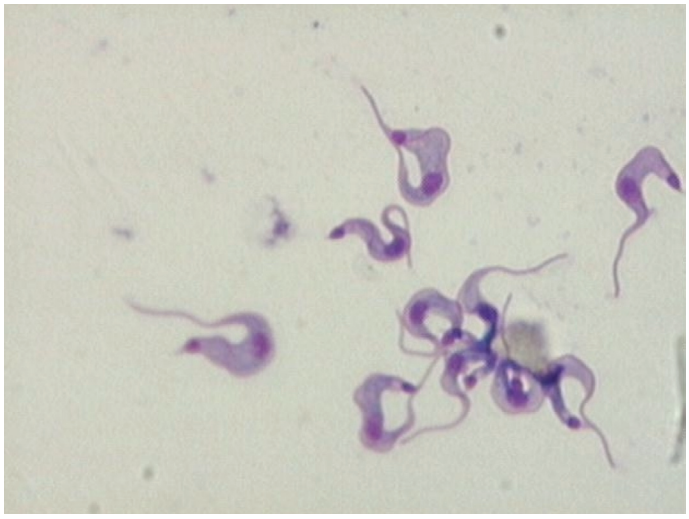

Fig. 1 - *Trypanosoma cruzi* trypomastigote forms in cerebrospinal fluid (Leishman, 40X).

DISCUSSION

DEL CASTILLO *et al.*[12] reported in 1990, for the first time, the association of central nervous system (CNS) Chagas disease and HIV infection. FERREIRA *et al.*[14], one year later, described the first case in Brazil.

To date, approximately 90 cases have been described of Chagas disease reactivation in AIDS patients, especially in Brazil and Argentina. However, a detailed description has only been given for a small number of these. The majority of cases were communicated in specialized congresses and symposiums[18,20]. The inclusion of Chagas disease reactivation in the list of AIDS-defining illnesses in Brazil should lead to a significant increase in the number of such case reports.

Brain expansive lesions, with or without meningoencephalitis, constitute the most frequent neurological presentation of Chagas disease reactivation in AIDS patients[9,18]. The clinical and radiological manifestations are unspecific and common to several CNS opportunistic diseases in AIDS patients. In our hospital (Institute of Infectious Diseases Emílio Ribas, São Paulo, Brazil), when meningeal or meningoencephalitis syndrome predominates, the main diagnoses are cryptococcosis, tuberculosis, and syphilis. When brain expansive lesion syndrome predominates, the main diagnoses include toxoplasmosis, tuberculosis (tuberculomas and/or abscesses), and CNS primary lymphoma (Vidal & Penalva de Olivera, unpublished data). Consequently, it is necessary to maintain a high level of suspicion for Chagas disease. A detailed epidemiological history, including current and past residency in Chagas disease endemic areas, use of intravenous drugs, and blood or hemoderivative transfusion, is helpful in suggesting a diagnosis.

The laboratorial diagnosis of CNS Chagas disease reactivation included serology test for *T. cruzi*, direct examination of blood smears, neuroimages, and CSF analysis[16,22]. The greater or lesser contribution of the last two methods will depend upon the current neurological syndrome (brain expansive lesion or meningoencephalitis, respectively). It is important to emphasize that a positive result for blood culture and xenodiagnostic, should not be interpreted as absolute evidence of reactivation, in view of the positive results of these tests in chronic chagasic patients[16].

Direct examination of CSF specimens could be a useful method for early and rapid diagnosis. A typical presentation of chagasic meningoencephalitis includes mild lymphocytosis (< 100 cells/mL), low glucose levels, increased protein, and *T. cruzi* trypomastigote forms in the CSF centrifuged, or after staining techniques[9,18].

The majority of AIDS patients with Chagas disease reactivation present $CD4^+$ lymphocytes count < 200 cells/μL, similar to those observed in other AIDS opportunistic neurological diseases[18].

The current algorithms of brain expansive lesions management were carried out in Chagas disease non-endemic areas[2,23]. Classically, if the images show one or more expansive lesions, it is recommended to initiate anti-*Toxoplasma* specific therapy for 10 to 14 days. A lack of therapeutic response after this period indicates the need for carrying out stereotaxic biopsy. In certain circumstances, a surgical approach must be precipitated, such as in patients with negative IgG serology for *T. gondii* and single brain lesion, or when indicated at the therapeutic level[2]. However, high levels of suspicion of alternative cerebral toxoplasmosis diagnoses, as has been already reported in one case of cytomegaloviruses[5] and in another of brain tuberculous abscess[29], could also indicate the need for early biopsy. Interestingly, MONTERO *et al.*[22] proposed a diagnostic algorithm for focal brain lesions in Chagas disease endemic areas.

Due to the high lethality, suspicion of Chagas disease reactivation must lead to more intensive diagnostic approaches, including early brain biopsy if it is not possible to reach the diagnostic through less invasive methods.

In recent years, the availability of molecular methods, applying the polymerase chain reaction (PCR) in CSF led to a shift from brain biopsy toward a "minimally invasive" approach of focal brain lesions in AIDS patients. This strategy helped to decrease the number of brain biopsies and augmented likelihood of *in vivo* diagnoses[3]. Recently, LAGES-SILVA *et al.*[21] reported an AIDS patient with chagasic meningoencephalitis diagnosed by PCR assay in CSF. Further studies are necessary in order to evaluate the application of molecular diagnosis in this clinical setting.

The lethality of Chagas disease reactivation in AIDS patients is very high. The majority of cases present a fatal course within 10-20 days after diagnosis[17]. However, suitable treatment could help to improve survival rates. Additionally, several case reports suggest that concomitant use of antiretroviral therapies and subsequent immunological reconstitution are vital for a more favorable outcome[16,17,28].

The inclusion of Chagas disease reactivation, as an AIDS-defining illness, should stimulate further physiopathological, epidemiological, and therapeutic studies on this important coinfection in the next few years. On the other hand, we expect that other endemic diseases, such as visceral leishmaniasis, could also be included.

In conclusion, Chagas disease reactivation must be considered in the differential diagnosis of meningoencephalitis, with or without focal brain lesions in AIDS patients. High levels of diagnostic suspicion, including epidemiological information (current or previous residency in Chagas disease endemic areas and/or use of intravenous drugs), clinical information (presence of concomitant myocardiopathy), and serological information (positive test for *T. cruzi* and/or negative for *T. gondii*), should lead to intensive diagnostic approaches. Emphasis should be placed on initiation of early therapy, which could reduce the case-fatality rate of this disease.

RESUMO

Meningoencefalite chagásica: relato de caso de doença recentemente incluida como indicativa de AIDS no Brasil

Recentemente, a reagudização da doença de Chagas (meningoencefalite e/ou miocardite) foi incluída na lista de doenças indicativas de aids no Brasil. Os autores relatam o caso de um paciente de 52 anos de idade, natural de área rural da Bahia e procedente de uma área urbana de São Paulo, sem história de doenças prévias e que apresentou meningoencefalite aguda. As sorologias e pesquisas parasitológicas diretas no sangue e no liquido cefalorraquideano (LCR) demonstraram presença de *Trypanosoma cruzi*, confirmando-se o diagnóstico mediante cultura do LCR. O teste rápido assim como os ELISA e Western Blot diagnosticaram infecção pelo vírus da imunodeficiência humana (HIV). Apesar do tratamento com benzonidazole e as medidas de suporte, o paciente faleceu 24 horas depois da admissão hospitalar. Em áreas endêmicas, a reagudização da doença de Chagas deve ser sempre considerada no diagnóstico diferencial das meningoencefalites e sua presença em pacientes com infecção pelo HIV é indicativa de aids.

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